

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference CLEV200023	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US04/21487	International filing date (<i>day/month/year</i>) 01 July 2004 (01.07.2004)	(Earliest) Priority Date (<i>day/month/year</i>) 12 September 2003 (12.09.2003)
Applicant CLEVELAND STATE UNIVERSITY		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found **unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (See Box No. III)

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material



a sequence listing



table(s) related to the sequence listing

b. format of material



in written format



in computer readable form

c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in computer readable form



furnished subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
MARK E. BANDY
FAY, SHARPE, FAGAN, MINNICH & MCKEE, LLP
1100 SUPERIOR AVENUE, SUITE 700
CLEVELAND, OH 44114

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) **18 JUL 2004**

Applicant's or agent's file reference

FOR FURTHER ACTION
See paragraph 2 below

CLEV200023

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US04/21487

01 July 2004 (01.07.2004)

12 September 2003 (12.09.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 38/00, 38/36; C07K 4/12, 14/745 and US Cl.: 530/300, 345

Applicant

CLEVELAND STATE UNIVERSITY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

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Commissioner for Patents
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Authorized officer

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SANDRA E. SAUCIER
PRIMARY EXAMINER

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/21487

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☒ in computer readable form

c. time of filing/furnishing

☒ contained in international application as filed.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/21487

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
- ☐ paid additional fees
- ☐ paid additional fees under protest
- ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
- ☒ not complied with for the following reasons:
- See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-8, 10, 43-49 and 51

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>2-5</u>	YES
	Claims <u>1, 6-8, 10, 43-49, 51</u>	NO
Inventive step (IS)	Claims <u>2-5</u>	YES
	Claims <u>1, 6-8, 10, 43-49, 51</u>	NO
Industrial applicability (IA)	Claims <u>1-8, 10, 43-49, 51</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1, 6-8, 10, 43-49, and 51 lack novelty under PCT Article 33(2) as being anticipated by Hortin (1990). The claims are drawn to peptides having a specific sequence that is identical to a portion of human Factor Va. In some dependent claims, this sequence is DYDY or DYDYQ. In some dependent claims, the peptide is claimed to demonstrate a specific level of inhibition of Factor Va. Some dependent claims are drawn to compositions comprising said peptide and analogues that mimic said peptide. In some dependent claims, various tyrosine (Y) residues are sulfonated.

Hortin (1990) teaches fragments of Factor Va comprising the sequence DYDYQ in which various Y residues are sulfonated (Figure 6, p. 950). Because Claim 1 recites "a peptide having a sequence identical to SEQ ID NO:10", it is interpreted as being broadly drawn to any peptide having the sequence DYDY, which includes Factor Va itself. In other words, claim 1 can be interpreted as being drawn to Factor Va, which is not novel.

Claims 2-5 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest peptides with specific activities against Factor Va activity, i.e. IC₅₀ values.

Claims 1-8, 10, 43-49, and 51 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 6, 7, 10, and 51 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s):

Claims 6 and 7 claim a peptide that "exhibits" a specific amino acid sequence. It is not clear whether "exhibits" refers to a function of the peptide or simply to one of its physical properties.

Claims 10 and 51 recite a peptide "analogue" that "mimics" the peptide of claims 1 and 43, respectively, but they do not particularly point out what characteristics are being "mimicked" by the "analogue". For example, the analogue could mimic the sequence, structure, function, or some other property of the peptide of claims 1 and 43. Additionally, it is not clear to what class of chemical "analogue" refers.

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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-8, 10, 43-49, and 51, drawn to a peptide with a sequence comprising SEQ ID NO. 10 and compositions comprising said peptide.

Group II, claim(s) 9, 50, 82-86, and 92-101, drawn to methods of treatment comprising administering the product of Group I.

Group III, claim(s) 11-18, 20, 52-58, and 60, drawn to a peptide with a sequence comprising SEQ ID NO. 11 and compositions comprising said peptide.

Group IV, claim(s) 19, 59, 87-91, and 102-111, drawn to methods of treatment comprising administering the product of Group III.

Group V, claim(s) 21-24, 26, 61-64, and 66, drawn to a peptide with a sequence comprising SEQ ID NO.s 12, 13 and compositions comprising said peptide.

Group VI, claim(s) 25 and 65, drawn to methods of treatment comprising administering the product of Group V.

Group VII, claim(s) 27-29, 31, and 67-69, drawn to a peptide with a sequence comprising SEQ ID NO. 14 and compositions comprising said peptide.

Group VIII, claim(s) 30 and 70, drawn to methods of treatment comprising administering the product of Group VII.

Group IX, claim(s) 32-35, 37 71-74, and 76, drawn to a peptide with a sequence comprising SEQ ID NO.s 7, 8 and compositions comprising said peptide.

Group X, claim(s) 36 and 75, drawn to methods of treatment comprising administering the product of Group IX.

Group XI, claim(s) 38-40, 42, 77-79, and 81, drawn to a peptide with a sequence comprising SEQ ID NO. 9 and compositions comprising said peptide.

Group XII, claim(s) 41 and 80, drawn to methods of treatment comprising administering the product of Group XI.

The inventions listed as Groups I-XII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: they are not unified by a special technical feature. PCT Rule 13.2 defines a "special technical feature" as a technical feature that defines a contribution that each claimed invention, considered as a whole, makes over the prior art.

The claims are drawn to six peptides and methods for using them. The product claims are broadly drawn to peptides comprising specific 4- and 5-amino acid sequences, said sequences being found in the human blood clotting factor Va. The use of the open-language term "having" includes all peptides comprising these sequences, regardless of their overall length. The product claims therefore read on Factor
Form PCT/ISA/210 (extra sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/21487

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/00, 38/36; C07K 4/12, 14/745
US CL : 530/300, 345

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 530/300, 345

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
US-PATS, US-PGUBS, CAPLUS, BIOSIS, MEDLINE, WPIDS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HORTIN, G.L. Sulfation of Tyrosine Residues in Coagulation Factor V. Blood, 1 September 1990, Vol 76, No 5, pages 946-952, especially page 950.	1, 6-8, 10, 43-49, 51
X, P	BECK, D.O., et al. The contribution of amino acid region ASP695-TYR698 of factor V to procofactor activation and factor Va function. Journal of Biological Chemistry, 23 January 2004, Vol 279, No 4, pages 3084-3095.	1-8, 10, 43-49, 51
A	PITTMAN, D.D., et al. Posttranslational sulfation of factor V is required for efficient thrombin cleavage and activation and for full procoagulant activity. Biochemistry, 7 June 1994, Vol 33, No 22, pages 6952-6959, especially page 6956.	1-8, 10, 43-49, 51
A	HORTIN, G.L., et al. Allosteric changes in thrombin's activity produced by peptides corresponding to segments of natural inhibitors and substrates. Journal of Biological Chemistry, 15 April 1991, Vol 266, No 11, pages 6866-6871, especially pages 6866 and 6867.	1-8, 10, 43-49, 51
A	PREVIERO, A., et al. Specific sulfonation of tyrosine, tryptophan, and hydroxy-amino acids in peptides. Biochimica et Biophysica Acta, 14 December 1979, Vol 581, No 2, pages 276-282, especially page 276.	1-8, 10, 43-49, 51



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A"	document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

17 March 2005 (17.03.2005)

Date of mailing of the international search report

18 JUL 2005

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